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Page 1

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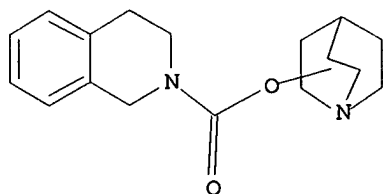
FILE COVERS 1967 - 10 Jul 1998 VOL 129 ISS 2  
FILE LAST UPDATED: 10 Jul 1998 (980710/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L1 STR



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L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1998 ACS ✓

ACCESSION NUMBER: 1998:35996 CAPLUS

DOCUMENT NUMBER: 128:114881

TITLE: Preparation of quinuclidine-containing  
isoquinolines and muscarine M3 receptor  
antagonists containing them

INVENTOR(S): Naito, Ryo; Takeuchi, Makoto; Okamoto,  
Yoshinori; Ikeda, Masaru; Isomura, Yasuo

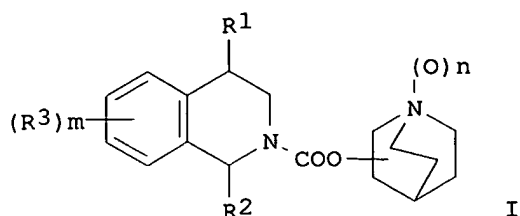
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

	NUMBER	DATE
PATENT INFORMATION:	JP 10007675 A2	980113 Heisei
APPLICATION INFORMATION:	JP 96-162221	960621

DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 OTHER SOURCE(S): MARPAT 128:114881  
 GI



AB Isoquinolines I (R1 = OH, lower alkoxy, lower alkyl; R2 = aryl, cycloalkyl, heterocyclyl; R3 = halo, OH, lower alkoxy, CO2H, lower alkoxy, lower acyl, etc.; m = 0-3; n = 0, 1) or their salts, useful as muscarine M3 receptor antagonists, are prepd. (+-)-Trans-1-phenyl-1,2,3,4-tetrahydro-4-isoquinolinol (0.28 g) was treated with 0.28 g (3R)-3-quinuclidinyl chloroformate.HCl at room temp. for 2.5 h to give 0.15 g trans-(1S,3'R,4S)- and trans-(1R,3'R,4R)-I (R1 = OH, R2 = Ph, R3 = H, n = 0). I was tested for in vitro muscarine receptor affinity and in vivo antagonistic activity.

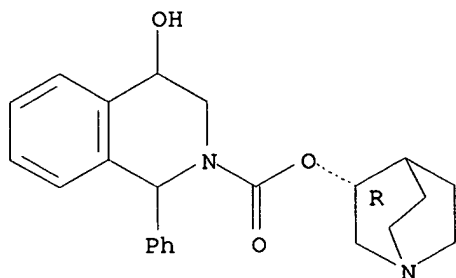
IT 201660-36-8P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of quinuclidine-contg. isoquinolines as muscarine M3 receptor antagonists)

RN 201660-36-8 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-4-hydroxy-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, [2(R)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 1998 ACS

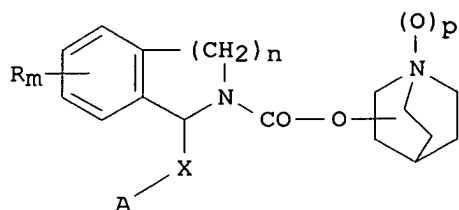
ACCESSION NUMBER: 1996:516723 CAPLUS

DOCUMENT NUMBER: 125:167804

TITLE: Preparation of new quinuclidine derivatives as muscarinic M3 receptor antagonists

INVENTOR(S): Takeuchi, Makoto; Naito, Ryo; Hayakawa, Masahiko; Okamoto, Yoshinori; Yonetoku, Yasuhiro; Ikeda, Ken; Isomura, Yasuo  
 PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 75 pp.  
 CODEN: PIXXD2

	NUMBER	DATE
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PATENT INFORMATION:	WO 9620194 A1	960704
DESIGNATED STATES:	W: AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG	
APPLICATION INFORMATION:	WO 95-JP2713	951227
PRIORITY APPLN. INFO.:	JP 94-327045	941228
DOCUMENT TYPE:	Patent	
LANGUAGE:	Japanese	
OTHER SOURCE(S):	MARPAT 125:167804	
GI		



I

AB Quinuclidine derivs. I [ring A = optionally substituted aryl, cycloalkyl, cycloalkenyl, heteroaryl contg. 1 to 4 heteroatoms selected from among oxygen, nitrogen and sulfur, or 5- to 7-membered satd. heterocycle; X = single bond or methylene; R = halo, hydroxy, lower alkoxy, carboxy, lower alkoxy carbonyl, lower acyl, mercapto, lower alkylthio, sulfonyl, lower alkylsulfonyl, sulfinyl, lower alkylsulfinyl, sulfonamido, lower alkanesulfonamido, carbamoyl, thio-carbamoyl, mono- or di(lower alkyl)carbamoyl, nitro, cyano, amino, mono- or di(lower alkyl)amino, methylenedioxy, ethylenedioxy or lower alkyl optionally substituted by halogeno, hydroxy, lower alkoxy, amino or mono- or di(lower alkyl)amino; p = 0 or 1; m = integer of 1 to 3; n = integer of 1 or 2], their salts, N-oxides, or quaternary ammonium salts, having an antagonistic effect on muscarinic M3 receptors and are useful as a preventive or remedy for urol. diseases, respiratory diseases or digestive diseases, are prepd. Thus, Et 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate (prepn. given) was reacted with 3-quinuclidinol in toluene contg. NaH at 140.degree. for 2 days to give the title compd. 3-quinuclidinyl 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate isolated as the oxalate salt. In an in vitro study, I had Ki values of 10<sup>-3</sup> to 10<sup>-10</sup> M against muscarinic M3 receptors.

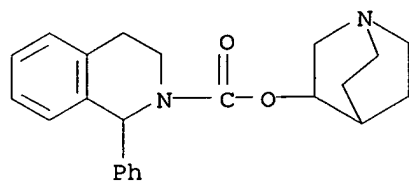
IT 180272-14-4P 180272-15-5P 180272-16-6P

180272-17-7P 180272-19-9P 180272-20-2P  
 180272-21-3P 180272-23-5P 180272-24-6P  
 180272-25-7P 180272-26-8P 180272-27-9P  
 180272-28-0P 180272-29-1P 180272-30-4P  
 180468-37-5P 180468-38-6P 180468-39-7P  
 180468-40-0P

RL: BAC (Biological activity or effector, except adverse); SPN  
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (prepn. of new quinuclidine derivs. as muscarinic M3 receptor  
 antagonists)

RN 180272-14-4 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,  
 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



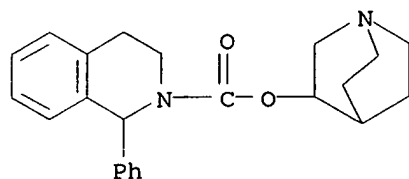
RN 180272-15-5 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,  
 1-azabicyclo[2.2.2]oct-3-yl ester, ethanedioate (1:1) (9CI) (CA  
 INDEX NAME)

CM 1

CRN 180272-14-4

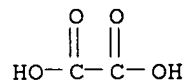
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CM 2

CRN 144-62-7

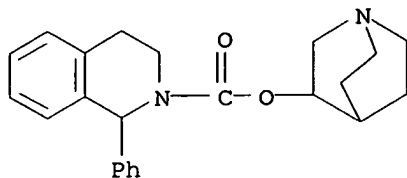
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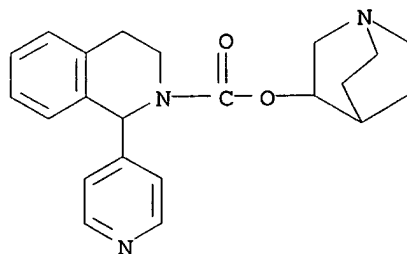
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,  
 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride (9CI) (CA

INDEX NAME)



● HCl

RN 180272-17-7 CAPLUS  
 CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-(4-pyridinyl)-,  
 1-azabicyclo[2.2.2]oct-3-yl ester, dihydrochloride (9CI) (CA INDEX  
 NAME)

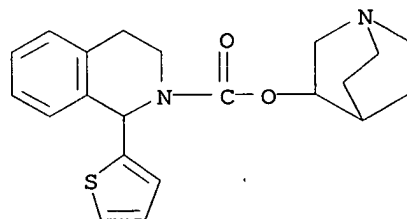


● 2 HCl

RN 180272-19-9 CAPLUS  
 CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-(2-thienyl)-,  
 1-azabicyclo[2.2.2]oct-3-yl ester, ethanedioate (1:1) (9CI) (CA  
 INDEX NAME)

CM 1

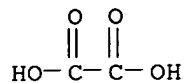
CRN 180272-18-8  
 CMF C21 H24 N2 O2 S



CM 2

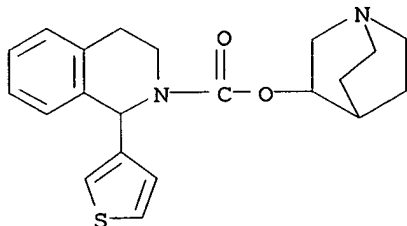
CRN 144-62-7

CMF C2 H2 O4



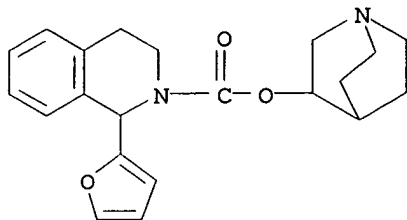
RN 180272-20-2 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-(3-thienyl)-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-21-3 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 1-(2-furanyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



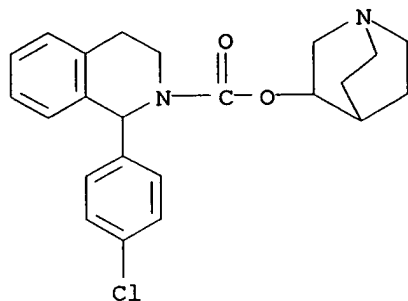
RN 180272-23-5 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-chlorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester, (E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 180272-22-4

CMF C23 H25 Cl N2 O2



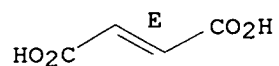
CM 2

CRN 110-17-8

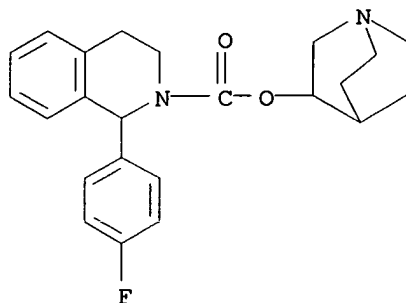
CMF C4 H4 O4

CDES 2:E

Double bond geometry as shown.

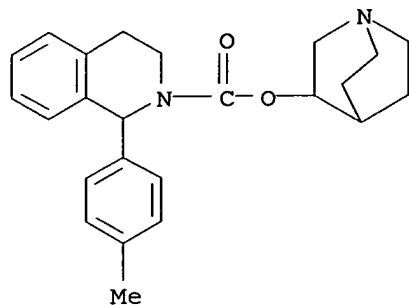


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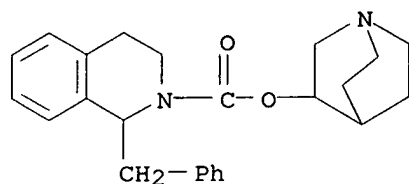
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-fluorophenyl)-3,4-dihydro-,  
1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)

RN 180272-25-7 CAPLUS

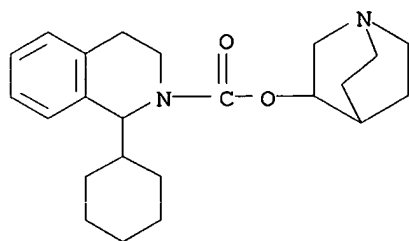
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-(4-methylphenyl)-,  
1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-26-8 CAPLUS  
 CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-(phenylmethyl)-,  
 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



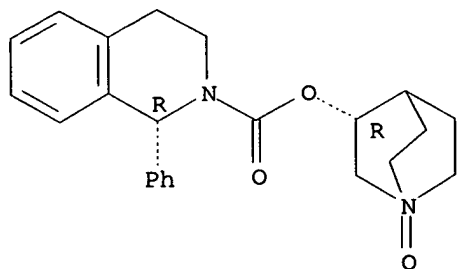
RN 180272-27-9 CAPLUS  
 CN 2(1H)-Isoquinolinecarboxylic acid, 1-cyclohexyl-3,4-dihydro-,  
 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-28-0 CAPLUS  
 CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,  
 1-oxido-1-azabicyclo[2.2.2]oct-3-yl ester, [R-(R\*,R\*)]- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.

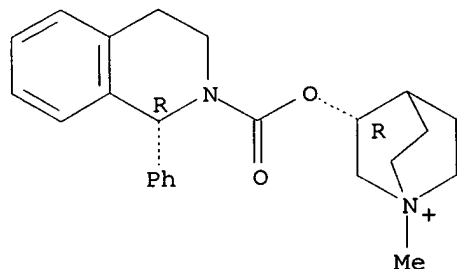




RN 180272-29-1 CAPLUS

CN 1-Azoniabicyclo[2.2.2]octane, 3-[[ (3,4-dihydro-1-phenyl-2(1H)-isoquinolinyl)carbonyl]oxy]-1-methyl-, iodide, [R-(R\*,R\*)]- (9CI)  
(CA INDEX NAME)

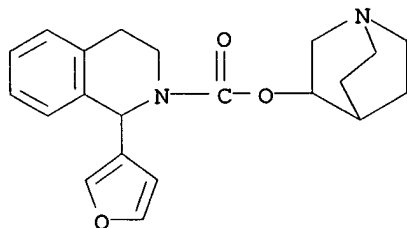
Absolute stereochemistry.



● I<sup>-</sup>

RN 180272-30-4 CAPLUS

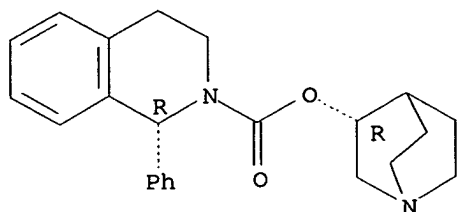
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(3-furanyl)-3,4-dihydro-,  
1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180468-37-5 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,  
1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R\*,R\*)]-  
(9CI) (CA INDEX NAME)

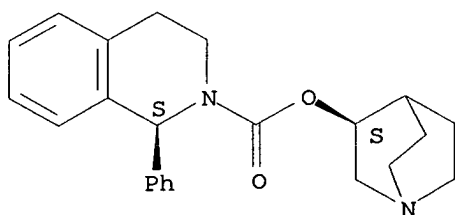
Absolute stereochemistry. Rotation (+).



● HCl

RN 180468-38-6 CAPLUS  
 CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,  
 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R\*,R\*)]-  
 (9CI) (CA INDEX NAME)

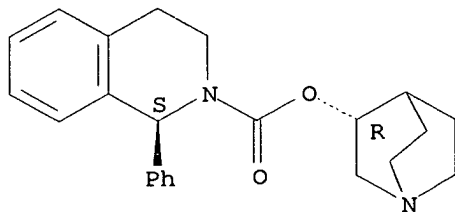
Absolute stereochemistry. Rotation (-).



● HCl

RN 180468-39-7 CAPLUS  
 CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,  
 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R\*,S\*)]-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

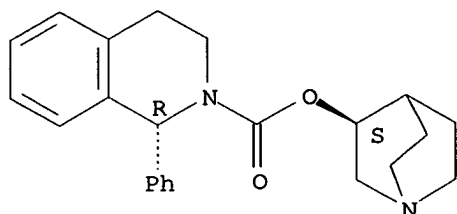


● HCl

RN 180468-40-0 CAPLUS  
 CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,

1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R\*,S\*)]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

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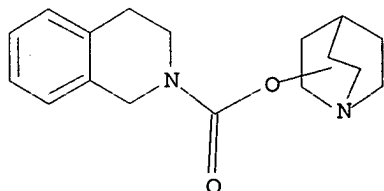
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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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STR



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